established treatment. It is supplied as a lyophilized powder which is dissolved in sterile water. The initial intravenous dose for children and adults is 1 mg per kg of body weight, repeated as necessary for persistent physiological and metabolic abnormalities up to a cumulative dose of 10 mg per kg of body weight. The average cumulative intravenous dose required to abort the clinical manifestations in humans is 2.5 mg per kg of body weight. Dantrolene given orally in doses of 1 to 2 mg per kg of body weight four times a day for one to three preoperatively may be prophylactic in known malignant hyperthermia reactors. There are no reported side effects with short-term dantrolene therapy.

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Hazards of Discontinuing Drugs Before Anesthesia

RESERPINE THERAPY for hypertension used to be discontinued before elective operations. Now it is felt that there is less anesthetic risk to hypertensive patients if this medication is continued up to the time of the surgical procedure. In fact, some danger of excessive cardiovascular stress arises if, inadvertently, antihypertensive therapy is not continued. On the other hand, the *Physician's Desk Reference* suggests that drugs such as monoamine oxidase inhibitors, tricyclic antidepressants and propranolol should be discontinued preoperatively. Because discontinuation of these drugs is not without hazard (such as depression, suicide, angina or myocardial infarction), the benefits and risks must be carefully weighed.

Few patients receive monoamine oxidase inhibitors. Their interaction with indirect-acting amines is widely recognized and generally avoidable. Further, their interaction with meperidine, resulting in coma, hyperpyrexia and hypertension, although not understood, is also avoidable. However, only a minority of anesthetists view continuing a regimen of monoamine oxidase inhibitors as desirable because the adverse effects are difficult to manage.

Unlike the monoamine oxidase inhibitors, the tricyclic antidepressants do not appear to cause severe adverse effects. While they potentiate the cardiovascular effects of exogenous catecholamines, this interaction can be avoided or controlled. Tachyarrhythmia has been reported following the simultaneous administration of the neuromuscular blocking agent pancuronium (Pavulon) in combination with the inhalation anesthetic agent halothane (Fluothane) to patients receiving long-term imipramine (Imavate, Presamine or Tofranil) therapy. Because this combination of drugs usually can be avoided, tricyclic antidepressants in therapeutic doses can be safely continued perioperatively. However, it should be noted that continuation of tricyclic antidepressants restricts the choice of anesthetic agents.

An initial series of case reports on patients undergoing cardiac operations seemed to support the view that propranolol (Inderal) interacted adversely with inhalation anesthetic drugs to produce severe myocardial depression and impaired ability to respond to cardiovascular stresses such as hemorrhage. However, reports of rebound phenomena after withdrawal of propranolol soon appeared. In hypertensive patients, abrupt withdrawal of propranolol was followed by 2 to 15 days of hypersensitivity to catecholamines. However, the course of hypersensitivity is such that it permits operations to be done within 48 hours of withdrawal. In patients with severe coronary disease and angina, exacerbation of coronary insufficiency symptoms and even acute myocardial infarction and death have been reported. This "rebound" may be the result of continued physical activity or emotional stress on a heart that is no longer protected by the beta-adrenergic blocking drug. In a large controlled study of coronary artery bypass graft patients, those who continued to receive propranolol up to the day of the operation did as well as the patients in whom propranolol therapy was discontinued. It should be noted that these study patients had intensive cardiovascular monitoring and specialists in cardiac anesthesia overseeing their anesthetic care. Nevertheless, if a surgical patient does not have the signs of excessive beta receptor blockade (bradycardia), continuation of propranolol administration does not appear to present unusual difficulties.

Antihypertensive agents should be given up to the time of operation. Clonidine (Catapres), however, presents a special problem because it has a

short elimination half-time (8.5 hours) and is not available in parenteral form. In several case reports, perioperative hypertension occurred in patients after clonidine therapy was discontinued. However, in one controlled study only two out of ten patients had hypertension after clonidine was withheld preoperatively. The hypertensive response, if it occurs, can be managed with hydralazine or sodium nitroprusside. One group of investigators has recommended preoperative withdrawal of clonidine and propranolol, when they are given together, and substitution of hydralazine.

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Pharmacological Prophylaxis Against Acid Aspiration

THE RISK of pulmonary aspiration of gastric contents associated with general anesthesia is of major concern. The inhalation of gastric juice with a pH of less than 2.5 and in a volume exceeding 0.3 ml per kg of body weight results in a severe and intense respiratory distress syndrome. Maneuvers to protect and isolate the airway have been developed; however, accidental aspiration from either reflux or active vomiting still ocurs. Therefore, pharmacological agents that will raise intragastric pH, hasten gastric emptying, elevate lower esophageal sphincter tone or decrease the volume of gastric secretion are being investigated.

Oral administration of antacid suspensions effectively raises intragastric pH and has become routine, if not obligatory, in patients at high risk for aspiration, such as pregnant women in labor. However, recent data suggest that aspiration of the antacid suspensions leads to a pulmonary syndrome as severe as acid aspiration itself, with more persistent pathological changes. Nevertheless, while clinical experience with antacid aspiration is limited and conflicting, the use of these agents in appropriate situations is still recommended.

Cimetidine, a gastric histamine H_2 receptor antagonist, substantially elevates gastric pH in many situations when used as a premedicant. It has gained widespread usage, but its efficacy and safety in pregnant women has not yet been confirmed. Further, it does not reliably decrease the volume of gastric contents in preoperative patients and it prolongs the action of some benzodiazepines.

Metoclopramide, a chlorbenzamide derivative will be available soon in the United States. It is an antiemetic agent that accelerates gastric emptying by sensitizing gastric smooth muscle to the action of acetylcholine, as well as having a direct autonomic effect. It has been shown to be effective in pregnant women in labor.

Domperidone, an investigational drug, is a benzimadazole antiemetic that elevates lower esophageal sphincter tone. This agent may have a useful application after further clinical trials are completed.

Reduction in the volume of gastric secretions has been partially successful with anticholinergic agents such as glycopyrrolate. Glypyrrolate also raises gastric pH in some patients. However, both glycopyrrolate and atropine decrease lower esophageal sphincter tone, thereby increasing the risk of reflux. This effect is antagonized by both domperidone and metoclopramide.

Meticulous attention to securing the airway mechanically is the key to the prevention of aspiration pneumonia. However, the use of one or more of the above pharmacological agents may provide extra protection to patients at high risk for aspiration.

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High Frequency Ventilation

TRADITIONAL MECHANICAL VENTILATION involves cuffed endotracheal tubes and large tidal volumes (12 to 15 ml per kg of body weight) given at slow rates (8 to 15 breaths per minute), with or without positive end-expiratory pressure (PEEP). It has been extremely successful in optimizing oxygenation in patients with serious lung disease, but it has serious drawbacks due to the high air-